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VDS-22

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : Not yet assigned
 Group : 1645
 Applicants : Christian Plank et al.
 Application No. : 10/023,317
 Filed : December 17, 2001
 For : COMBINATIONS FOR INTRODUCING NUCLEIC ACIDS
 INTO CELLS

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Confirmation No. : 2272

New York, New York
 March 28, 2002

Hon. Commissioner for Patents
 P.O. Box 2327
 Arlington, VA 22202

SUPPLEMENTAL PRELIMINARY AMENDMENT

Sir:

Prior to the issuance of the first Office Action in the above-identified application, kindly amend the application as follows:

04/03/2002 HGEREH1 00000096 10023317

01 FC:203 9.00 OP

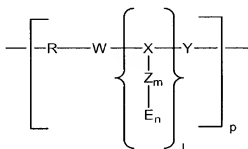
08/01/2002 Y6IZAW 00000001 061075 10023317

01 FC:203 54.00 CH

IN THE SPECIFICATION

Replace the paragraph from page 4, line 4 to page 6, line 1 with the following:

The present invention relates in its first aspect to a charged copolymer having the general formula I



wherein R is an amphiphilic polymer or a homo- or hetero-bifunctional derivative thereof,

and wherein X

- i) is an amino acid or an amino acid derivative, a peptide or a peptide derivative or a spermine or a spermidine derivative; or
- ii) wherein X is



wherein

a is H or, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkyl;

and wherein

b, c and d are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iii) wherein X is



wherein

a is H or, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkyl,

and wherein

b and c are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iv) wherein X

is a substituted aromatic compound with three functional groupings W₁Y₁Z₁,

wherein W, Y and Z have the meanings mentioned below;

wherein

W, Y or Z are the same or different groups CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH₂;

and wherein the effector molecule E is a cationic or anionic peptide or peptide derivative or a spermine or spermidine derivative or a glycosaminoglycane or a non-peptidic oligo/polycation or -anion; wherein m and n are independently of each other 0, 1 or 2; wherein

p preferably is 3 to 20; and wherein

l is 1 to 5, preferably 1.

If l is > 1, the moiety X-Z_m-E_n is the same or different.

Replace the priority claim on page 1, on the first line of the application after the title with the following:

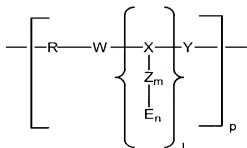
This application claims benefit under 35 U.S.C. §§ 120 and 365(c) from International Application No. PCT/EP00/05778, filed June 21, 2000, which was published in the German language.

IN THE CLAIMS

Replace claims 1, 5-9 and 12-14 with substitute claims 1, 5-9 and 12-

14 as follows:*

1. (Twice Amended) A combination of a carrier and a complex comprising a nucleic acid molecule and a charged copolymer of the general formula I

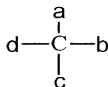


wherein R is an amphiphilic polymer or a homo- or hetero-bifunctional derivative thereof,

and wherein X

- i) is an amino acid or an amino acid derivative, a peptide or a peptide derivative or a spermine or a spermidine derivative; or

- ii) wherein X is



* Applicants enclose a "Version Showing Changes Made" including the amendments to the specification and to the claims.

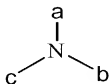
wherein

a is H or, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkyl; and

wherein

b, c and d are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iii) wherein X is



wherein

a is H or, optionally halogen or dialkylamino substituted, C₁-C₆ alkyl,

and wherein

b and c are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iv) wherein X

is a substituted aromatic compound with three functional groupings W₁Y₁Z₁,

wherein W, Y and Z have the meanings mentioned below;

wherein

W, Y or Z are the same or different groups CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH₂;

and wherein the effector molecule E

is a cationic or anionic peptide or peptide derivative or a spermine or spermidine derivative or a glycosaminoglycane or a non-peptidic oligo/polycation or -anion; wherein

m and n are independently of each other 0, 1 or 2; wherein

p preferably is 3 to 20; and wherein

I is 1 to 5.

5. (Twice Amended) The combination according to claim 1, wherein a ligand for a higher eukaryotic cell is coupled to the copolymer.
6. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the nucleic acid molecule is condensed with an organic polycation or cationic lipid molecule and the complex formed thereby has a charged copolymer of the general formula I bound to its surface via ionic interaction.

7. (Twice Amended) The combination according to any one of claims 1-3 and 5, containing a therapeutically effective nucleic acid molecule.
8. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the carrier consists of a biologically non-resorbable material.
9. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the carrier consists of a biologically resorbable material.
12. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the carrier is a carrier which is obtainable by cross-linkage of a copolymer as defined in claim 1.
13. (Twice Amended) A method of transferring a nucleic acid molecule into a cell comprising using the combination according to any one of claims 1-3 and 5.
14. (Twice Amended) A pharmaceutical composition comprising the combination according to any one of claims 1-3 and 5.
15. (Added) The combination according to claim 1, wherein I is 1.

REMARKS

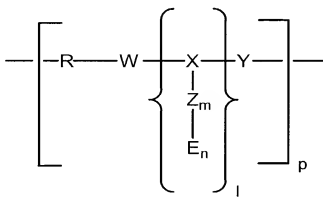
Applicants have amended the specification on page 5, lines 12-13 and claim 1 to correct an error that occurred during translation of the international application into English. Specifically, applicants have replaced "have" with "are."

VOS-22

Version Showing Changes Made

IN THE SPECIFICATION

The present invention relates in its first aspect to a charged copolymer having the general formula I

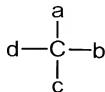


wherein R is an amphiphilic polymer or a homo- or hetero-bifunctional derivative thereof,

and wherein X

i) is an amino acid or an amino acid derivative, a peptide or a peptide derivative or a spermine or a spermidine derivative; or

ii) wherein X is



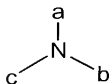
wherein

a is H or, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkyl;

and wherein

b, c and d are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iii) wherein X is



wherein

a is H or, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkyl,

and wherein

b and c are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iv) wherein X

is a substituted aromatic compound with three functional groupings W₁Y₁Z₁,

wherein W, Y and Z have the meanings mentioned below;

wherein

W, Y or Z [have] are the same or different groups CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH₂;

and wherein the effector molecule E

is a cationic or anionic peptide or peptide derivative or a spermine or spermidine derivative or a glycosaminoglycane or a non-peptidic oligo/polycation or -anion; wherein

m and n are independently of each other 0, 1 or 2; wherein

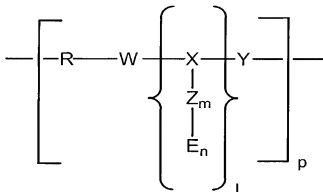
p preferably is 3 to 20; and wherein

l is 1 to 5, preferably 1.

If l is > 1, the moiety X-Z_m-E_n is the same or different.

IN THE CLAIMS

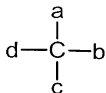
1. (Twice Amended) A combination of a carrier and a complex comprising a nucleic acid molecule and a charged copolymer of the general formula I



wherein R is an amphiphilic polymer or a homo- or hetero-bifunctional derivative thereof,

and wherein X

- i) is an amino acid or an amino acid derivative, a peptide or a peptide derivative or a spermine or a spermidine derivative; or
- ii) wherein X is



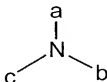
wherein

a is H or, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkyl; and

wherein

b, c and d are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iii) wherein X is



wherein

a is H or, optionally halogen or dialkylamino substituted, C₁-C₆ alkyl,

and wherein

b and c are the same or different, optionally halogen- or dialkylamino-substituted, C₁-C₆ alkylene; or

iv) wherein X

is a substituted aromatic compound with three functional groupings W₁Y₁Z₁,

wherein W, Y and Z have the meanings mentioned below;

wherein

W, Y or Z [have] are the same or different groups CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH₂;

and wherein the effector molecule E

is a cationic or anionic peptide or peptide derivative or a spermine or spermidine derivative or a glycosaminoglycane or a non-peptidic oligo/polycation or -anion; wherein

m and n are independently of each other 0, 1 or 2; wherein

p preferably is 3 to 20; and wherein

l is 1 to 5[, preferably 1].

5. (Twice Amended) The combination according to [any one of claims 1 to 3] claim 1, wherein a ligand for a higher eukaryotic cell is coupled to the copolymer.
6. (Twice Amended) The combination according to any one of claims [1 to 3] 1-3 and 5, wherein the nucleic acid molecule is condensed with an organic polycation or cationic lipid molecule and the complex formed thereby has a charged copolymer of the general formula I bound to its surface via ionic interaction.
7. (Twice Amended) The combination according to any one of claims [1 to 3] 1-3 and 5, containing a therapeutically effective nucleic acid molecule.

8. (Twice Amended) The combination according to any one of claims [1 to 3] 1-3 and 5, wherein the carrier consists of a biologically non-resorbable material.
9. (Twice Amended) The combination according to any one of claims [1 to 3] 1-3 and 5, wherein the carrier consists of a biologically resorbable material.
12. (Twice Amended) The combination according to any one of claims [1 to 3] 1-3 and 5, wherein the carrier is a carrier which is obtainable by cross-linkage of a copolymer as defined in claim 1.
13. (Twice Amended) A method of transferring a nucleic acid molecule into a cell comprising using [a] the combination according to any one of claims [1 to 3] 1-3 and 5.
14. (Twice Amended) A pharmaceutical composition comprising [a] the combination according to any one of claims [1 to 3] 1-3 and 5.